

## Remarks

### I. Status of the Application and Claims

At the time the above-captioned application entered into prosecution in the United States, it had a total of 18 claims. In a Preliminary Amendment filed on May 21, 1998, Applicants deleted claims 13-16 and amended claims 3-5, 8-10, 12, 17 and 18. On December 18, 1998, Applicants made additional amendments to claims 1, 5-7, 8, 12 and 17. In the present response, claims 7, 10 and 12 have been amended.

### II. The Amendments

The amendments made herein either correspond exactly to an amendment suggested by the examiner (claim 7) or correct an obvious grammatical error (claims 10 and 12). These amendments clearly do not add new matter to the application. Moreover, they serve to obviate the examiner's rejection of claims under 35 U.S.C. § 112, second paragraph, thereby narrowing the issues for appeal. In light of these considerations, Applicants submit that the amendments are proper and it is respectfully requested that they be entered.

### III. Submission of U.S. 4,188,373

A copy of United States patent 4,188,373 is enclosed with the present response. Applicants submit that this reference demonstrates unequivocally that methods for making thermoreversible gels were well known in the art for at least 20 years prior to the filing of the present application.

## The Rejections

### I. Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

On page 2 of the Office Action, the examiner rejects claim 7 based upon the allegation that the word "is" renders the claim unclear. It is suggested that the word "comprises" would overcome the rejection. Since Applicants have amended claim 7 in exactly the manner suggested, it is respectfully submitted that this rejection has been obviated.

Claims 10 and 12 are also rejected on page 2 of the Office Action based upon the presence of the phrase "any of one claims 1-7." Applicants have amended these claims to read

"any one of claims 1-7." In light of this amendment, it is submitted that the examiner's rejection has been overcome and it is respectfully requested that this rejection be withdrawn.

## **II. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph**

On page 2 of the Office Action, the examiner rejects claims 1-12 and 17-18 under 35 U.S.C. § 112, first paragraph. It is alleged that:

Claims 1-12, 17-18 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for the examples of the specification prepared as disclosed on page 7, does not reasonably provide enablement for the invention as amended. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with the broad claims. EP 455 396, U.S. 5,635,540 and 4,780,320 disclose that compositions comprising one or more local anaesthetics in oil form, one or more surfactants having thermoreversible gelling properties and water form single phase gel or cream compositions. Applicants have not claimed the limitations which would yield an oil in water emulsion and distinguish the instant claims over the prior art.

Applicants respectfully traverse this rejection.

In the response filed by Applicants on December 18, 1998, claim 1 was amended to indicate that the compositions formed must be an emulsion or microemulsion and have thermoreversible gelling properties. An emulsion is formed when one liquid distributes in small globules throughout the body of a second liquid. Contrary to the examiner's allegations, all of the elements necessary to form an emulsion and distinguish the composition claimed from those in the prior art are present in amended claim 1. Specifically, there is a first liquid made up of local anesthetics in oil form; a second liquid, water, that is immiscible with the first; and surfactants present in an amount sufficient to produce a homogenous formulation, *i.e.*, present at a sufficient concentration to cause the oil to disburse evenly throughout the water. The requirement that an emulsion or microemulsion be formed is itself a limitation which can serve to distinguish prior art.

Only one of the references cited by the examiner, U.S. 5,635,540, describes a composition in which anaesthetics are used to produce a single phase gel or cream.<sup>1</sup> The fact that the compositions disclosed are a single phase whereas Applicants' claimed compositions are an emulsion or microemulsion is sufficient to distinguish this reference. Although the reason for the different forms that the compositions take is not entirely clear, it may be related either to the way that the compositions are prepared or to the relative concentration of surfactant used. In the latter regard, it should be noted that the '540 specification suggests that, depending upon the type of surfactant used, 20 to 50 weight percent should be used, with a preferred concentration being between 30 and 40 weight percent (see column 3, lines 62-67). Applicants' compositions tend to use an amount of surfactant that is either outside that range or at the extreme lower end. For example, in the eight compositions described in detail on pages 8-11, the following concentrations of surfactant were used: examples 1 and 2, 21%; example 3, 17.5%; examples 4-6, 16%; example 7, 22.5%; and example 8, 25.3%.

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The other two references cited by the examiner are also clearly distinguishable. EP 455 396 does disclose single phase systems, but none of these contain oil in water preparations. It appears that an emulsion is not formed simply because there are not two immiscible liquids present in preparations. Similarly, the '320 patent does not disclose oil in water solutions, but rather a system in which drug is released from microparticles or microcarriers. Thus, Applicants submit that, contrary to the allegations in the Office Action, the claimed compositions may be distinguished from those in the prior art based upon elements that are recited in the claims. Moreover, one of ordinary skill in the art clearly would be capable of titrating a surfactant into an oil in water preparation and determining the point at which an even dispersion is obtained. Applicants have given eight examples of specific emulsions that can be formed, but many others are clearly possible. In light of such guidance and the knowledge existing in the art, Applicants submit that claim 1 is fully enabled with respect to emulsion or microemulsion formation.

In addition, it is respectfully submitted that the formation of thermoreversible gels has been practiced in the art for over 20 years and clearly requires no more knowledge than that

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<sup>1</sup> It is repeatedly emphasized in the patent that the composition forms a single phase (see column 1, lines 7-15; column 2, lines 50-60; column 3, lines 62-67; and column 4, lines 42-45).

possessed by one of average skill in the art. Applicants are enclosing herewith U.S. 4,188,373 as evidence for the long standing knowledge of procedures for the formation of thermoreversible gels. Again, numerous examples and other teachings are provided in the application that would provide additional guidance for the making of the claimed preparations.

In light of the above considerations, Applicant respectfully submit that the rejection of claims under 35 U.S.C. § 112, first paragraph, is unwarranted. It is therefore respectfully requested this rejection be withdrawn. If the examiner maintains the rejection, it is requested that the specific reasons why the claims have been alleged as non-enabled be set forth. In other words, it is respectfully requested that the examiner explain exactly why one of skill in the art could not make and use the claimed compositions.

### Conclusion

Applicants submit that each and every one of the examiner's rejections have been overcome by the amendments and arguments above. It is therefore respectfully requested that these rejections be withdrawn. Applicants submit that the present application is now in condition for allowance and earnestly solicit early notice of such favorable action.

If, in the opinion of the examiner, a phone call may help to expedite prosecution of this application, the examiner is invited to call Applicants' undersigned attorney at (202) 639-6585.

Respectfully submitted,  
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